

Pharmacological and Phytochemical Evidences for the Extracts from Plants of the Genus *Vitex* – A Review

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ABSTRACT

The scientific basis for the statement that plants and their active constituents play an important role in the prevention diseases is continuously advancing. In fact, the origin of many therapeutic substances from the genus *Vitex*. The genus *Vitex* contains 270 species distributed around the world. It is an interesting source of potential bioactive molecules, as iridoids compounds, flavonoids, diterpenoids derivatives, phytosteroids, with antioxidant, anti-inflammatory, antimicrobial, Hepatoprotective activity, analgesic and antihistamine, Anti-implantation, antiasthmatic activities. This work reviews the pharmacological evidence of extracts of plants from the genus *Vitex*, giving an overview of the most studied biological effects and the known phytochemical composition. Although more studies are necessary, *Vitex* exhibits proven potential to become of important pharmacological interest.

Keywords: genus *Vitex*, Pharmacology, phytochemistry, antioxidant, Medicinal plants.

INTRODUCTION

In recent times, focus on plant research has increased all over the world, and a large body of evidence has been collected to show the immense potential of medicinal plants used in traditional systems. Various medicinal plants have been identified and studied using modern scientific approaches. The results revealed the potential of medicinal plants in the field of pharmacology. [1-3] The genus *Vitex* approximately includes 270 known species of trees and shrubs within tropical and sub-tropical regions, although few species may be found in temperate zones. *Vitex trifolia* L. is a shrub or shrubby tree that may grow up to 6 m. Its origin is unknown and several varieties have been described in distant countries as India and Mexico. [4] Several *Vitex* species are used as folk remedies in Mexico. *Vitex mollis* is reported as a remedy to alleviate dysentery, as well as an analgesic and anti-inflammatory medicine; other folk uses include the treatment of scorpion stings, diarrhea and stomach ache. [5] Other *Vitex* species are folk remedies to treat diarrhea and gastrointestinal affections (*V. pyramidalis*, *V. pubescens*, *V. agnus-castus* and *V. gaumeri*). [6-7] Also, antimalarial, antimicrobial, and antifungal properties have been reported for *V. gaumeri*, *V. agnus-castus* and *V. negundo*, respectively; *V. negundo* is also used as an anti-inflammatory agent, *Vitex negundo*

(Family: *Verbenaceae*), is an important medicinal plant found throughout India. The all of its parts are used in Ayurvedic and Unani systems of medicine, the extracts from its leaves and roots are the most important in the field of medicine and drug. Its leaves [8] and seeds [9] are widely used externally for rheumatism and inflammations of joints and are also reported to have insecticidal properties. Internally, decoction of its leaves is taken as diuretic, expectorant, vermifuge, tonic and febrifuge. The chemical components of the essential oil of leaf isolated from *Vitex negundo* and other species while *Vitex gaumeri* is used to treat colds and coughing spells. [10-11] It is well known that a considerable number of plant species, besides their popular use as medicine in many countries, In India some species are present *Vitex glabrata*, *Vitex leucoxydon*, *Vitex penduncularis*, *Vitex pinnata*, and *Vitex trifolia* [12] possess insecticidal activities. The genus *Vitex* sp. is not an exception. *V. negundo* has larvicidal activity against the mosquito species *Culex quinquefasciatus* and *Anopheles stephensi* [13], and acts as a deterrent to the mosquito *Aedes aegypti* [14] *Vitex rotundifolia* also shows deterrent properties towards *A. aegypti*. Several other *Vitex* species are currently being investigated in specific programs of pest control. [15-17]

Vitex agnus-castus

Vitex agnus-castus L. (*Verbenaceae*) is a small tree or shrub, which is widely distributed along the Anatolian coastal lane. [18] This plant has important medicinal properties and is especially used for treatment of premenstrual problems and hyperprolactinemia because of its hormone-like effect. [19-21] In Anatolian folk medicine, *Vitex agnus-castus* is used as

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diuretic, digestive, antifungal and also against anxiety, early birth and stomachache. [22-23] *Vitex agnus-castus* contains iridoids [24], Flavonoids [25-27], Diterpenoids [28], essential oils [29] and ketosteroids. [30] *Vitex agnus-castus* is a medicinal plant with a long tradition in folk medicine as an aphrodisiac, anti-oestrus cycle effect, diseases, stomachache, relieves pain, eupeptic, emmenagogous, antispasmodic, aperitif, soporific action, mastopathies, galatogogous, activity against P388 leukemia cells, inhibition of prolactin synthesis and inhibitor for dopamine D₂ and opioid. [31-37] The methanolic extract of the flowering stems of *Vitex agnus-castus* yielded three new iridoids: 6'-*O*-foliamenthoylmussaenosidic acid (agnucastoside A), 6'-*O*-(6,7-dihydrofoliamenthoyl)mussaenosidic acid (agnucastoside B) and 7-*O*-trans-p-coumaroyl-6'-*O*-trans-caffeoyl-8-epiloganic acid (agnucastoside C) in addition to four known iridoids (aucubin, agnucastoside, mussaenosidic acid and 6'-*O*-*p*-hydroxybenzoylmussaenosidic acid) and one known phenylbutanone glucoside (myzodendrone). [38] The dried ripe fruit of *Vitex agnus-castus* L. is widely used for the treatment of premenstrual syndrome [39] (Fig. 1).

The chemical composition and antioxidant activity of the essential oil and different solvent extracts of *Vitex agnus castus*. GC and GC-MS analysis was resulted in the detection of 27 components of the oil. Major components of the oil were 1, 8-cineole, sabinene, α -pinene, α -terpinyl acetate and (*Z*)- β -farnesene. Antioxidant activities of the samples were determined by three different test systems, DPPH, β -carotene/linoleic acid and reducing power assays. In all systems, water extract exhibited excellent activity potential than those of other extracts (hexane, dichloromethane, ethyl acetate and methanol) and the oil. As expected, amount of total phenolics was very high in this extract. Dichloromethane extract has been found to be rich in flavonoids. A positive correlation was observed between the antioxidant activity potential and total phenolic and flavonoid levels of the extracts. [40]

The essential oils of *Vitex agnus-castus* were evaluated against Vth instar larvae of *Spilosoma obliqua*, when applied topically on the dorsal side of mesothoracic region, for insect growth regulatory activity. This treatment caused extended larval period and pupal period, increase in larval mortality and adult deformity and decrease in adult emergence, fecundity of female and egg fertility of test insect. [41] From the fruits of *Vitex agnus-castus* L. one new diterpene, 6 β , 7 β -diacetoxy-13-hydroxy-labda-8, 14-diene, as well as two previously described diterpenes rotundifuran and vitexilactone (Fig. 2) were isolated. All obtained diterpenoids belong to the labdane type. The structures determinations were mainly based on 1D and 2D NMR spectra and MS data interpretation. 6 β , 7 β - diacetoxy-13-hydroxy-labda-8, 14-diene and rotundifuran showed an affinity to the dopamine-D₂-receptor. [42] Compound vitexilactone identified by 1D and 2D NMR data and the MS spectrum and comparison of its spectroscopic data. Compound vitexilactone was isolated before from the leaves of *Vitex cannabifolia* [43] and the fruits of *Vitex rotundifolia* Linn. [44] All of the physical and spectroscopical data were identical with those of rotundifuran described in the literature. [45]

A novel labdane diterpene alkaloid, vitexlactam A (Fig. 3) was isolated as a prism from the *n*-hexane extract of the fruits of *Vitex agnus-castus* through normal and reverse phase column chromatography. Its structure was elucidated to be

6 β -acetoxy-9 α -hydroxy-13(14)-labden-16, 15-amide, based on chemical and spectral evidences including 1D and 2D NMR spectra. The structure was confirmed by X-ray crystallographic analysis. Compound vitexlactam A is the first naturally occurring labdane diterpenoid containing α , β -unsaturated γ -lactam moiety. [46]

Extract of *Vitex agnus castus* in the treatment of women suffering from premenstrual syndrome (PMS) with moderate to severe complaints. [47] Investigate the efficacy and safety of *Vitex agnus castus* extract in Chinese women suffering from moderate to severe premenstrual syndrome. [48] Four new flavonoids, luteolin 6-C-(4"-methyl-6"-*O*-trans-caffeoylglucoside), luteolin 6-C-(6"-*O*-trans-caffeoylglucoside), luteolin 6-C-(2"-*O*-trans-caffeoylglucoside), and luteolin 7-*O*-(6"-*p*-benzoylglucoside), together with four known ones 5, 4'-dihydroxy-3, 6, 7, 3-tetramethoxyflavone, luteolin, artemetin and isorhamnetin, were isolated from the root bark of *Vitex agnus-castus*. The structures were elucidated by spectroscopic means. [49]

A methanol extract of *Vitex agnus-castus* L. was tested for its ability to displace radiolabeled estradiol from the binding site of estrogen receptors alpha (ER α) and beta (ER β). Progesterone receptor was upregulated in the Ishikawa endometrial cancer cell line. However, chaste-tree berry extract did not induce estrogen-dependent alkaline phosphatase activity in Ishikawa cells. Bioassay-guided isolation, utilizing ER binding as a monitor, resulted in the isolation of linoleic acid as one possible estrogenic component of the extract. The use of pulsed ultrafiltration liquid chromatography-mass spectrometry, which is an affinity-based screening technique, also identified linoleic acid as an ER ligand based on its selective affinity, molecular weight, and retention time. Linoleic acid also stimulated mRNA ER β expression in T47D:A18 cells, PR expression in Ishikawa cells. [50] The antiepileptic activity of hydrophilic extract of *Vitex agnus castus* fruit (*Vitex*) was evaluated by the kindling model of epilepsy. Intact male rats were stereotaxically implanted with a tripolar and two monopolar electrodes in amygdala and dura, respectively. These results indicate that *Vitex* can reduce or prevent epileptic activity as demonstrated by reduction of after discharge duration and length of convulsion in a dose dependent manner. In conclusion, *Vitex* at appropriate dose can probably reduce or control epileptic activities. [51]

The essential oils from leaf and fruit of *Vitex agnus castus* for menopausal balance were conducted. Surveys completed by the some participants in that trial indicated strong symptomatic relief of common menopausal symptoms. The result of the second round of trials, which were conducted with more additional subjects under the supervision of health practitioners. The second trial appears to support the finding of the first trial, as well as identifying some important contraindications to use of the essential oil. [52] Subjects who mixed essential oil *vitex* with any form of progesterone supplementation (including progesterone cream) consistently noted breakthrough bleeding. Any woman who is concurrently taking any form of hormone replacement therapy should be closely monitored by a health professional when *vitex* is introduced. [53-54]

Extracts of *Vitex agnus-castus* are used for the treatment of premenstrual symptoms. The mechanism of action was proposed to be dopaminergic and estrogenic in nature. To

isolate these endocrinologically active substances, receptor ligand binding assays and cell cultures were used as *in vitro* systems to monitor the bioactivity-guided chromatographic separation. The fraction with the highest dopaminergic activity was a mixture of diterpenes of the clerodane type. These newly isolated diterpenes inhibited cAMP formation and PRL-release in rat pituitary cell cultures. The estrogenic compounds were identified as the flavonoids penduletin and apigenin. Both substances are specific ligands for the ER β . Using the strategy of bioactivity-guided fractionation we were able to isolate new dopaminergic diterpenes with a high specific activity which contributes significantly to the PRL-lowering activity of *Vitex agnus-castus*. The therapeutical potential of the ER β specific ligands penduletin and apigenin needs further investigation. Starting material for the isolation of single constituents was the *Vitex agnus-castus* extract which was obtained by extracting finely ground *Vitex agnus-castus* seeds with aqueous ethanol 70 % (v/v) and smoothly drying in vacuum^[55] (Fig. 4). Ethanol extract of the dried ripe fruit of *Vitex agnus-castus* displays cytotoxic activity against certain kinds of human cancer cell line resulting in the induction of apoptosis. In this paper, we investigate the molecular mechanism of apoptosis induced by *Vitex* using a human gastric signet ring carcinoma cell line, KATO-III. DNA fragmentation was observed in *Vitex*-treated KATO-III cells in a time- and dose-dependent manner. Results demonstrate that intracellular oxidative stress and mitochondrial membrane damage is responsible for *Vitex*-induced apoptosis, which may be mediated by a diminution of reduced type glutathione within the cell.^[56]

Vitex agnus castus extract inhibits prolactin release which is caused by selective stimulation of pituitary dopamine receptors of the D₂-type.^[57-58] In clinical investigations and double-blind trials with preparations containing *Vitex agnus castus* extract, a decrease of latent and pathologically increased prolactin levels and an influence on prolactin release in healthy subjects has been demonstrated.^[59-64] In a placebo-controlled, randomized, double-blind study the efficacy of a *Vitex agnus castus* extract containing solution was investigated in patients suffering from cyclical mastalgia. Patients had mastalgia on at least 5 days in the pre-treatment cycle. During this cycle and during treatment the intensity of mastalgia was recorded once per cycle using a visual analogue scale. *Vitex agnus castus* extract appears effective and was well tolerated and further evaluation of this agent in the treatment of cyclical mastalgia is warranted.^[65]

***Vitex trifolia* Linn**

Vitex trifolia L. (*Labiatae*) is a tropical shrub widespread in Pacific-Asian countries such as India, Sri Lanka, China, Philippines, Indonesia, North Australia, New Caledonia and French Polynesia. It has also been reported from East Africa and introduced to many islands in the Central Pacific and Hawaii.^[66] The anti-inflammatory potential of an aqueous extract of *Vitex trifolia* leaves was evaluated by monitoring its effects on the modulation of cytokines, the mediators of inflammation, as well as on the expression profiles of inducible nitric oxide synthase which produces the free radical nitric oxide.^[67]

Vitex trifolia L. (*Labiatae*) appears as one of the popular herbal medicine in the Pacific region. The leaves are employed in maceration or decoction, internally or externally in baths to cure Ciguatera Fish Poisoning-related pruritus.^[68-69] *Vitex trifolia* is used to treat various disorders like fever,

inflammation, health care, and increase in body weight, nematocidal activity and anti-tumor activity.^[70-74]

Biological assays of *Vitex trifolia* L. organic extracts have shown relevant activities. Hexanic and dichloromethanolic extracts, when prepared from stems and foliage, have proved to be very toxic against several cancer cell lines in culture. Also, an important antifeeding activity against the insect pest *Spodoptera frugiperda* (Lepidoptera: Noctuidae) was recorded. The hexanic extract from leaves completely inhibited the growth of the fungal plant pathogen *Fusarium* sp.^[75] The essential oils of *Vitex trifolia* were evaluated against Vth instar larvae of *Spilosoma obliqua*, when applied topically on the dorsal side of mesothoracic region, for insect growth regulatory activity. This treatment caused extended larval period and pupal period, increase in larval mortality and adult deformity and decrease in adult emergence, fecundity of female and egg fertility of test insect.^[76] An abietane-type diterpene, named vitetrifolin A, and two labdane-type diterpenes, named vitetrifolins B and vitetrifolin C, were isolated from the acetone extract of the fruits of *Vitex trifolia* L. along with three known diterpenes, rotun-difuran, dihydrosolidagenone and abietatriene 3 β -ol. The structures of these compounds were elucidated on the basis of spectroscopic analysis, X-ray crystallographic analysis and chemical evidence^[77] (Fig. 6). The petroleum ether and ethanol extracts of *Vitex trifolia* leaves exhibited moderate inhibiting activity against both gram-positive and gram-negative bacteria.^[78]

Vitex cymosa

Vitex cymosa Bertero is a small tree widely distributed in the Central and Amazon regions of Brazil, where it is popularly known as Taruma-do-Igapo and Taruma-do-alagado. A new ecdysteroid, 26-hydroxypinnatasterone, together with 20-hydroxyecdysone, was isolated from the stem barks of *Vitex cymosa*.^[79]

Vitex polygama

The species *Vitex polygama* Cham. is found mainly in the states of Bahia, Minas Gerais and Rio de Janeiro and the bark and fruits of this plant are traditionally used as emenagogue and diuretic. The 20-Hydroxyecdysone, ajugasterone C, ajugasterone C monoacetonide and turkesterone were isolated from the branches of *Vitex polygama*.^[80]

Vitex canescens

Vitex canescens Kurz is a medium-sized tree scattered throughout the countryside of Thailand. A number of *Vitex* species have been investigated for ecdysteroids.^[81] Among the *Vitex* species reported to be endemic to Thailand, only two of them, *Vitex pinnata* and *Vitex glabrata*, were reported to contain 20-hydroxyecdysone (1) and turkesterone (2).^[82-83] The former plant species also contained pinnatasterone (3), an ecdysteroid lacking a C-22 hydroxyl group. In the isolation of 1 and 2, and a new ecdysteroid canescensterone (4), from the bark of *V. canescens*^[84] (Fig. 5). 20-hydroxyecdysone and turkesterone, a new ecdysteroid, canescensterone, was isolated from the bark of *Vitex canescens*. A new ecdysteroid, 24-epi-abutasterone, was isolated from the root bark of *Vitex canescens*. 20-Hydroxyecdysone, 24-epi-makisterone A, shidasterone, calonysterone and turkesterone were also isolated from this plant species.^[85]

***Vitex negundo* Linn**

Vitex negundo Linn. Verbenaceae, known as Nirgundi in Hindi, grows gregariously in wastelands and is also planted

as a hedge-plant. It is an erect, 2–5 m in height, slender tree with quadrangular branchlets distributed throughout India. The leaves have five leaflets in a palmately arrangement, which are lanceolate, 4–10 cm long, hairy beneath and pointed at both ends. The bluish purple flowers are numerous. The fruit is succulent, black when ripe, rounded and about 4 mm in diameter. [86-87]

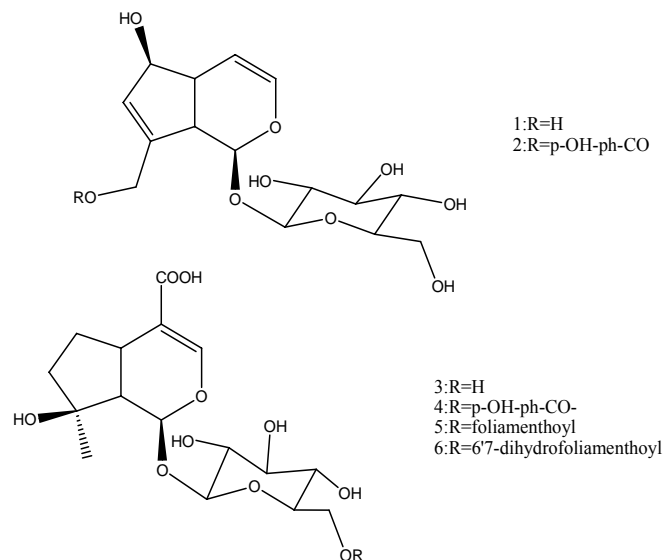


Fig. 1: Glucosides from *Vitex agnus-castus*(flowering stems)-Aucubin(1), Agnuside(2), Mussaenosidic acid(3), 6'-o-p-hydroxybenzoylmussaenosidic acid(4), 6'-o-p-foliamenthoymussaenosidic acid (agnucastoside A) (5), agnucastoside B (6)and also Agnucastoside C

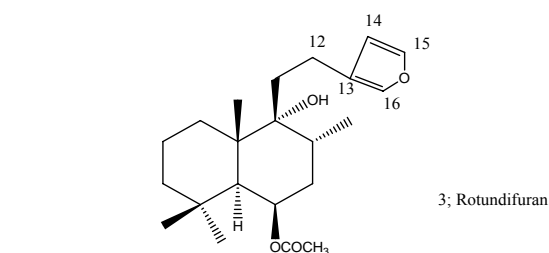
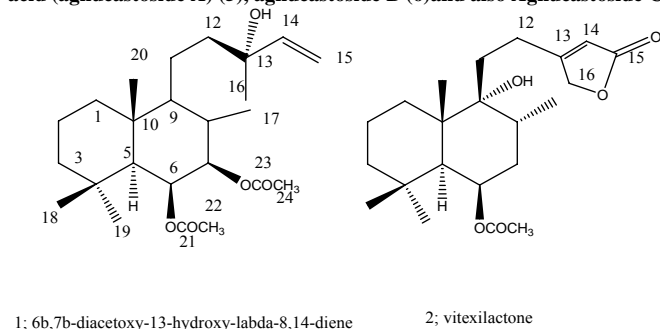


Fig. 2: Diterpenoids from the fruits of *Vitex agnus-castus*.

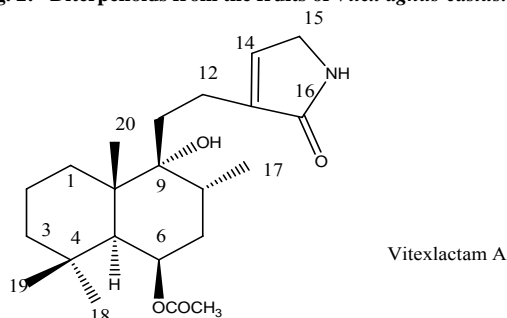


Fig. 3: labdane diterpene lactam from the fruits of *Vitex agnus-castus*

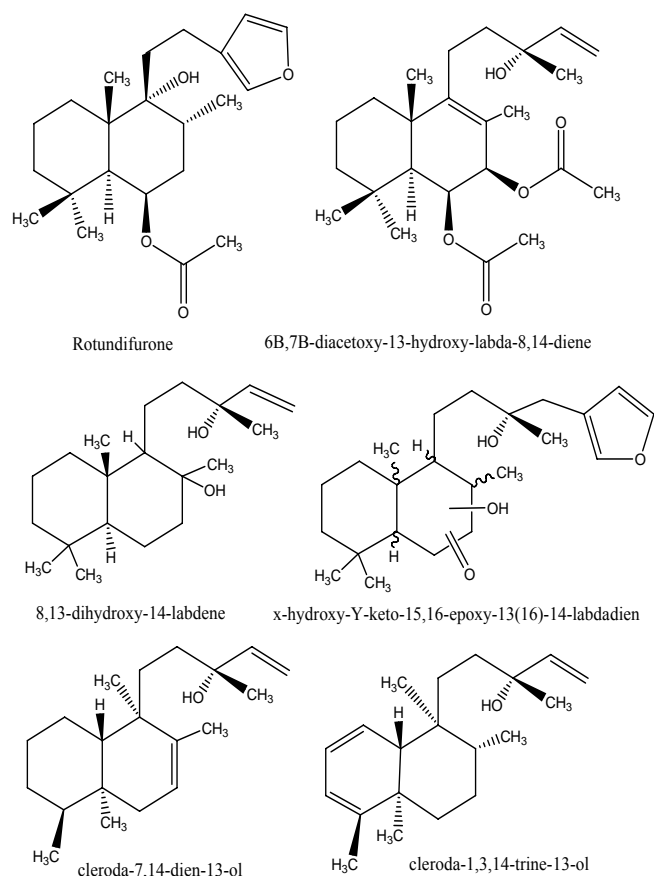


Fig. 4: bicyclic diterpene from *Vitex agnus-castus*

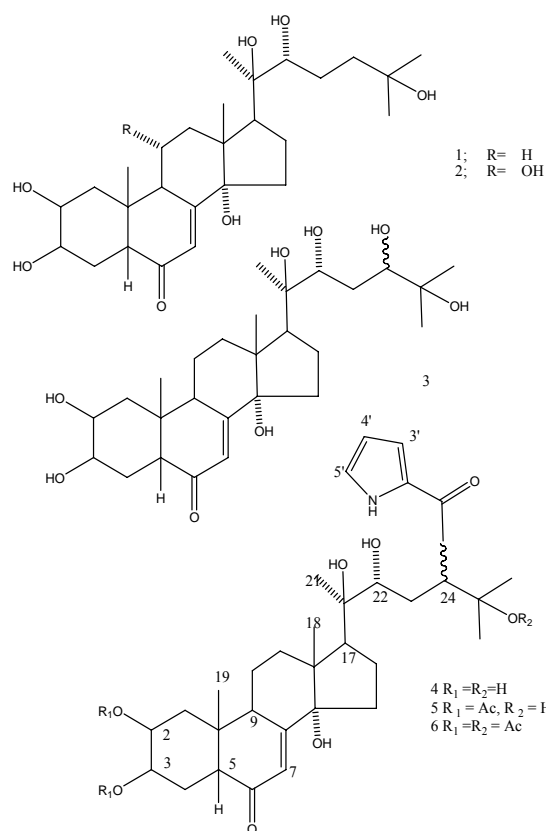


Fig. 5: Ecdysteroids From *Vitex Canescens*(from bark) 20-hydroxyecdysone(1), turkesterone(2), pinnatasterone(3), canescensterone(4), Canescensterone 2,3-diacetate (5), Canescensterone 2,3,25-triacetate (6).

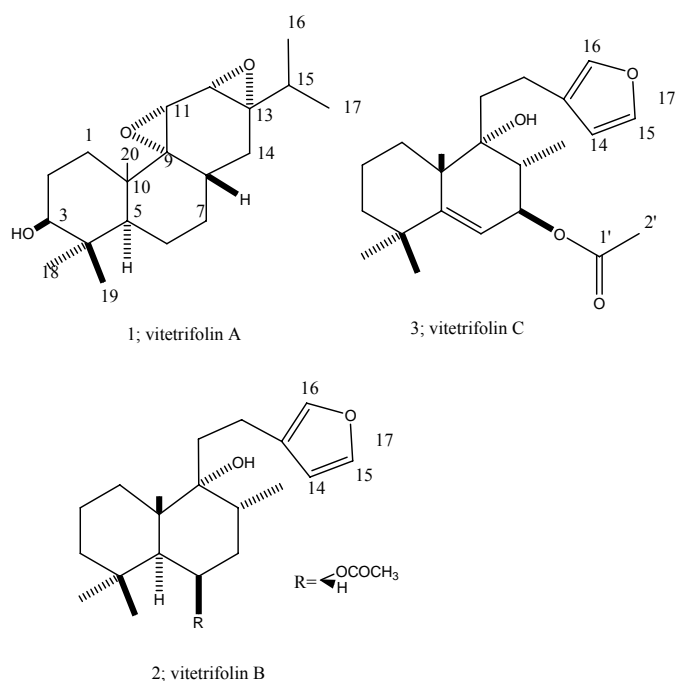
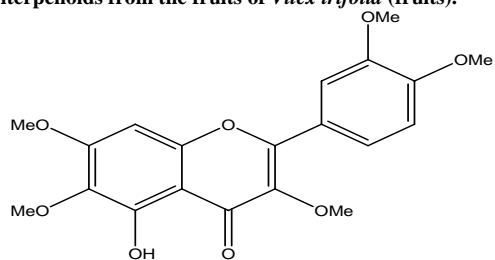
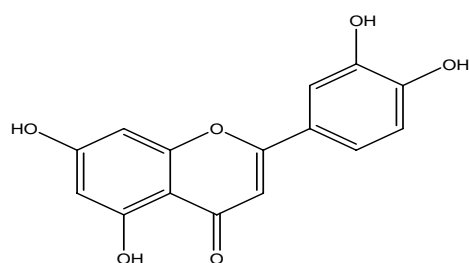


Fig. 6: Diterpenoids from the fruits of *Vitex trifolia* (fruits).



5-hydroxy-3,6,7-trimethoxy-2-(3,4-dimethoxyphenyl)-4H-chromen-4-one



5,7-dihydroxy-2-(3,4-dihydroxyphenyl)-4H-chromen-4-one

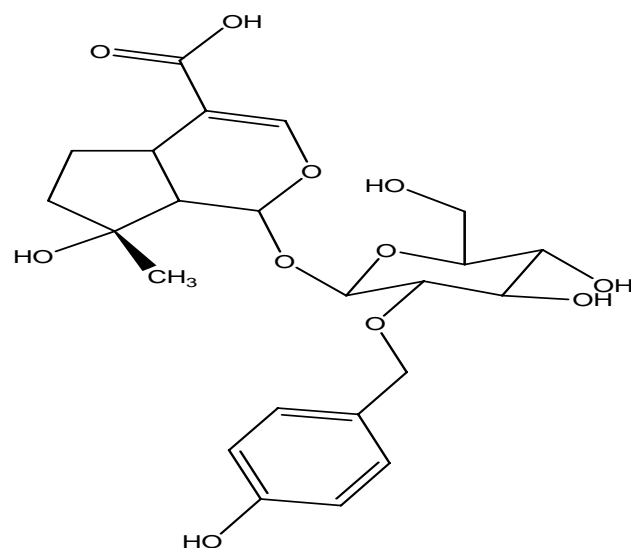
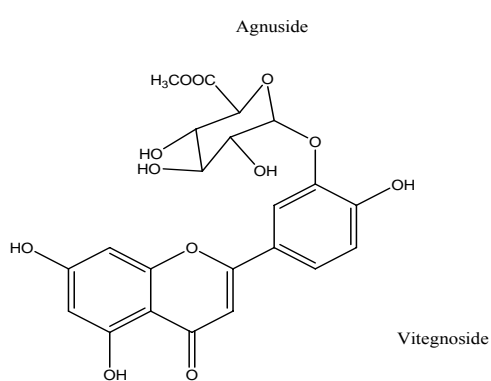
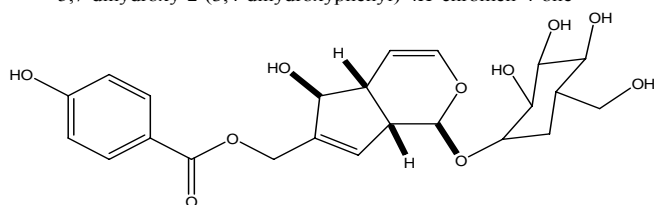


Fig.7: Phytochemical Constituents of the Leaf of *Vitex negundo* L.

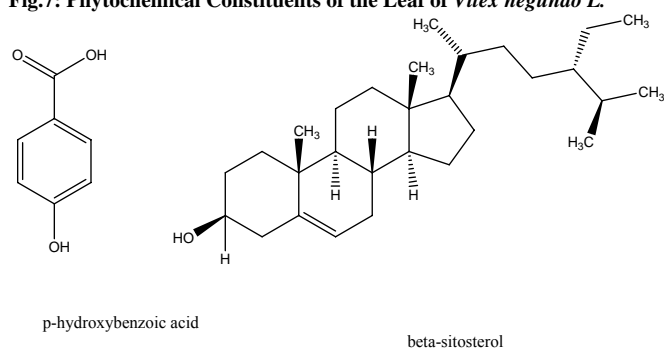


Fig. 8: Phytochemical Constituents of the Bark of *Vitex negundo* L

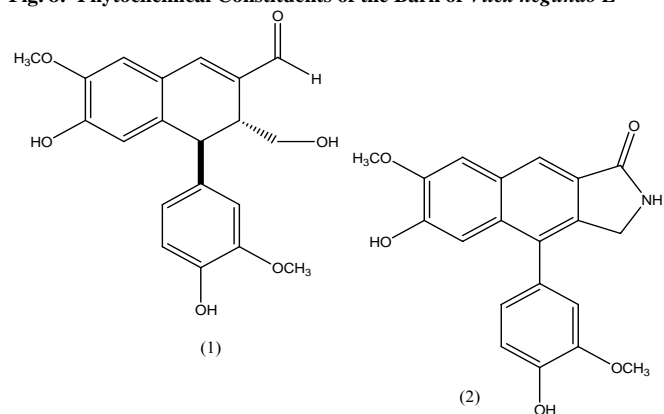


Fig. 9: Phytochemical Constituents of the Seeds of *Vitex negundo* L

Phytochemical studies on *Vitex negundo* have afforded several types of compounds, such as volatile oils [88-91], lignans [92-93], Flavonoids [94-96], iridoids [97-99], terpenes (triterpenes, diterpenes, sesquiterpenes) [100-101], and steroids. [102]

The most flavonoid glycoside from Leaves of *Vitex negundo* of Ethanolic extract is 5-hydroxy-3, 6, 7-trimethoxy-2-(3, 4-dimethoxyphenyl)-4H-chrome-4-on and 5, 7-dihydroxy-2-(3,4-dihydroxyphenyl)-4H-chromen-4-one. [103] Methanolic extract also contains, Negundoside, Agnuside, Vitenoside [104] (Fig. 7). Bark of *Vitex negundo* Linn. p-Hydroxybenzoic acid (1) and β -sitosterol (2) (Fig. 8) were isolated, and identified from the methanol and hexane extracts of *Vitex negundo*.

Table 1: Some Important Chemical Compounds found in the Vitex genus and its pharmacodinamic propertie.

Species	Important Compounds	Source Studied	Pharmacodinamic effect	Reference
Vitex negundo Linn	Leaves (1) 5-hydroxy-3,6,7-trimethoxy-(3,4-dimethoxyphenyl)-4H-chromen-4-one. (2) 5,7-dihydroxy-2-(3,4-dihydroxyphenyl)-4H-chromen-4-one (3) Negundoside (4) Agnuside (5) Vitegnoside	Ethanol extract	Antifungal	Maurya et al,2007
	Bark (1) p-Hydroxybenzoic acid (2) β -sitosterol	Methanolic extract		Gautam et al,2008
	Seeds (1) vitedoamine A	Methanol and hexane extracts		Dhakal RC et al, Vol. 23, 2009.
	Roots (1) lignans (agnucastoside A agnucastoside B) (agnucastoside C) (aucubin, agnuside, mussaenosidic (myzodendrone)	Acetoacetate fraction		Chawla et al, 1992.
		Methanol extract	Tyrosinase inhibitory	Malik A et al, 2006
		methanolic Extract of the flowering stems	Antimicrobial activity	Uz AK et al, 2003.
Vitex agnus-castus	1,8-cineole, sabinene , α -pinene , α -terpinyl acetate , and (Z)- b-farnesene.	Water and ethanol extracts of fruits	Antioxidant activity	Sarikurkcü C et al, 2009.
	6b,7b-diacetoxy-13-hydroxy-labda-8,14-diene and rotundi-furan Linoleic Acid	Hexane extracts of fruits	Affinity to the dopamine-D2-receptor	Stiche O et al, 1999.
	apigenin , 5-hydroxy-3,6,7,4-tetramethoxyflavone and casticin	Methanol Extract Of Fruits	Estrogenic	Farnsworth N R, et al,2004
Vitex canescens	pinnatasterone 24-O-(pyrrole 2-carboxylate)	Aqueous Ethanol Extract	Premenstrual Symptoms	Jarry H et al, 2006.
	24-epi-abutasterone,	n-hexane and Ethanol Extracts		Suksamrar A et al, 1994.
	vitetrifolin A, vitetrifolins B and C. rotundifuran, dihydrosolidagenone and abietatriene 3b-ol	Ethanol extract of the root bark		Suksamrar A et al, 1997.
Vitex trifolia		Acetone extract of the fruits		Ono M et al, 2000.
		petroleum ether and ethanol extracts	Activity against both gram-positive and gram-negative bacteria	Rahman E et al, 2001.
Vitex cymosa	ecdysteroid, 26 hydroxypinnatasterone , 20-hydroxyecdysone	Stem barks		Leit G et al, 2001.
Vitex peduncularis Wall	pachypodol, ursolic acid, 2 α -hydroxyursolic acid, vitexin	Leaves extraction		Riaz et al, 1990
Vitex pinnata Linn	pinnatasterone, together with 20-hydroxyecdysone and turkesterone	Bark of the plant	Pupariatio	Suksamrar A, 1993
Vitex leucoxydon Linn		Ethanol, aqueous extract of leaf	Depress spontaneous motor activity	Makwana et al, 1989.

From the seed of *Vitex negundo* L. The following compound Isolated acetoacetate fraction, two phenyl naphthalene-type lignans. (Fig. 9) were obtained and identified as 6-hydroxy-4-(4-hydroxy-3-methoxy-phenyl)-3-hydroxy-methyl-7-methoxy-3,4-dihydro-2-naphthaldehyde (1) and vitedoamine A (2), both of which have been previously reported and isolated from the seeds of *Vitex negundo*.^[77] Powdered roots are used for piles as a demulcent for dysentery. It also used in dyspepsia, colic, rheumatism, worms, boils and leprosy.^[105] The roots contain a furanoterpenophilane. They are used as an antidote to snake venom. Tyrosinase inhibitory lignin's from the methanol extract of the roots of *Vitex negundo* Linn.^[106]

Hepatoprotective activity of *Vitex negundo* leaves ethanolic extract was investigated against hepatotoxicity produced by administering a combination of three anti-tubercular drugs isoniazid -7.5 mg/kg, rifampin-10 mg/kg and pyrazinamide-35 mg/kg.^[76] *Vitex negundo* Linn. contains many polyphenolic compounds, terpenoids, glycosidic iridoids and alkaloids. Since polyphenolic compounds have high antioxidant potential, the antioxidant potency of *Vitex negundo* was investigated by employing various established in vitro systems, such as 2, 20-azino-bis 3-ethyl benzothiazoline-6-sulfuric acid /Lipid Peroxide /Superoxide/Hydroxyl radical scavenging and iron ion chelation.

The oral anti-inflammatory, analgesic and antihistamine properties of mature fresh leaves of *Vitex negundo* Linn. claimed in the Ayurvedic medicine by orally treating a water extract of the leaves to rats. The carrageenan-induced rat paw oedema was significantly suppressed in inversely dose-dependent manner^[8] anti-hyperglycemic activities.^[107] *Vitex negundo* exhibited significant activity against *E. coli*, *K. aerogenes*, *P. vulgaris* and *P. aerogenes* at all dosages. Extract of leaves of *V. negundo* showed activity against bacteria.^[108] Ethanolic extract and various fractions like petroleum ether, aqueous leaves of *Vitex negundo* were prepared. The antiasthmatic activity evaluated by various experimental models like mast cell degranulation.^[109] Anti-implantation activity of the methanolic extract of leaves of *Vitex negundo* Linn. Pregnant female mice.^[110] Xanthine oxidase inhibitory activity was assayed from *Vitex negundo*. The methanolic root extracts of *Vitex negundo* Linn. and *Emblica officinalis* Gaertn. were explored for the first time for anti snake venom activity. The plant (*Vitex negundo* and *Emblica officinalis*) extracts significantly antagonized the *Vipera russellii* and *Naja kaouthia* venom induced lethal activity both in vitro and in vivo studies.^[111] Petroleum ether extracts of the leaves of *Vitex negundo* were evaluated for larvicidal activity against larval stages of *Culex tritaeniorhynchus* in the laboratory.^[112] Crude aqueous extract of *Vitex negundo* Linn. leaves at investigated for laxative activity.^[113] Ethanolic extracts of *Vitex negundo* were taken for anthelmintic activity against Indian earthworm *Pheritima posthuma*.

***Vitex peduncularis* Wall**

The dried leaves on extraction yielded pachypodol, ursolic acid, 2 α -hydroxyursolic acid, vitexin and peduncularcin. In Orissa, a decoction of the leaves is taken as tea during cold season. Infusion of leaves administered intramuscularly or orally in Rabbits increases the osmotic resistance of cells and inhibits haemolysis by saponin, cobra venom, bile salts, or saline solution.^[114]

***Vitex pinnata* Linn**

An ecdysteroid, pinnatasterone, together with 20-hydroxyecdysone and turkesterone were isolated from the bark of the plant. Pinnatasterone showed low biological activity in the pupariation test with housefly larvae.^[81] The Flavonoids, luteolin, iso-orientin, and vitexin have been isolated from the flowers. In Brunei, the young leaf shoots are eaten raw to counter hypertension and fever. The shoots are also used for poulticing wounds. A root-tea is consumed for backache, bodyache and fatigue.^[115]

***Vitex leucoxylo* Linn**

Ethanolic extract and cold aqueous infusion of leaf were found to depress spontaneous motor activity. Both the extracts suppressed acetic acid induced writhing in mice and carrageenan-induced hind paw oedema in rats. Besides Ethanolic extract produced significant inhibition of granulation tissue formation while cold aqueous infusion decreased total serum cholesterol. In acute inflammation, cold aqueous infusion as well as a mixture of Flavonoids of *Vitex leucoxylo* Linn showed anti-inflammatory activity without any effect on chronic inflammation.^[116]

The main biological findings and the known phytochemical composition of the *Vitex* genus are summarised in Table 1. The studies conducted to date have demonstrated that the plants of the *Vitex* genus have the potential to provide biologically active compounds that act as antioxidants, anti-

inflammatory, antimicrobial, Hepato-protective activity, analgesic and antihistamine, Anti-implantation, antiasthmatic activities. Thus, the *Vitex* genus deserves additional evaluation as a provider of Hepatoprotective agents. Indeed, there is a current need for availability of new plant-derived bioactive molecules; thus genus *Vitex*. may be a great natural source for the development of new drugs and may provide a cost-effective mean of treating Heart problem and other diseases in the developing world.

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